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14. ABSTRACT The goal of this project is to develop a computer-aided diagnosis (CAD) system for automatic interval change analysis of microcalcification clusters on mammograms. Based on our regional registration method a local area on the prior that may contain the corresponding cluster is determined. A search program is used to detect cluster candidates within the local area. The cluster on the current image is then paired with the candidates to form true (TP-TP) or false (TP-FP) pairs. A correspondence classifier (CC) using automatically extracted features is designed to reduce the false pairs. A temporal classifier (TC) based on current and prior information is used if a cluster is detected in the prior, and a current classifier (CurC) based on current information alone is used if no prior cluster is detected. 175 temporal pairs of mammograms were used for evaluation. The search program detected 90.2% of the clusters on the priors with an average of 0.43 FPs/image. The CC identified 85% (149/175) of the TP-TP pairs with 15 false matches within the 164 image pairs that had detected clusters. The TC achieved a test Az of 0.83 for the 164 pairs for classifying the clusters as malignant or benign. For the 11 clusters without detection on the prior, the test Az by the CurC was 0.72. The radiologist achieved an Az of 0.72 for both the 175 and the 164 temporal pairs.

15. SUBJECT TERMS
Breast cancer, computer-aided diagnosis, screening, classification, image analysis

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(3) Table of Contents

(4) Introduction

Treatment of breast cancer at an early stage can significantly improve the survival rate of patients. Mammography is currently the most sensitive method for detecting early breast cancer, and it is also the most practical for screening. Although general rules for differentiation between malignant and benign lesions exist, in clinical practice, approximately only 15-30% of cases referred to surgical biopsy are actually malignant. A number of research groups are in the process of developing computer-aided diagnosis (CAD) methods which can provide a consistent and reproducible second opinion to the radiologist for the detection and classification of breast abnormalities.

Radiologists routinely compare mammograms from a current examination with those obtained in previous years, if available, for identifying interval changes, detecting potential abnormalities, and in evaluating breast lesions. It is widely accepted that interval changes in mammographic features are very useful for both detection and classification of abnormalities. However, CAD techniques that use multiple exams for detection or characterization have not been commonly explored, probably because of the difficulty in the registration of the compressed breast images from different exams. We have been investigating methods for analysis of temporal changes of masses on mammograms to improve detection and classification. To our knowledge, there is no existing CAD technique for registration of microcalcification clusters or classification of microcalcifications based on temporal change information.

The extraction of any meaningful information from a prior mammogram first requires a common frame of reference between the current and prior mammograms. Several complicating factors, such as breast compression difference between current and prior mammograms, energy difference between the two imaging conditions, differences in screen film properties and film processing conditions, and potential changes in breast structures between the two images with patient age, make it difficult to obtain such a frame of reference. On breast images, there are no invariant landmarks (except for the nipple) that can serve as control points in conventional image registration methods to register the two mammograms. In this project, we propose to develop an innovative regional registration method that does not depend on specific control points. We will first approximately align the current and prior mammogram based on maximization of mutual information. Next, we will design a novel approach in which the computer emulates the radiologists' search method in finding corresponding lesions on mammograms. Automated search of microcalcification cluster within the search region on the prior mammogram will be performed. Our current automated microcalcification detection algorithm will provide a basis for this search. However, since the detection is limited to the small search region, the detection can be performed in high resolution and the algorithm parameters can be adjusted to improve the detection sensitivity of the very subtle clusters on the prior mammograms without excessive trade-off in increasing false-positives. A correspondence classifier will be developed to identify the matched pair of clusters on the two mammograms. The image features of the corresponding microcalcification clusters can then be automatically extracted and feature measures characterizing interval changes derived. A classification scheme to differentiate malignant and benign clusters using the interval change information will be developed. This computerized interval change analysis will be an important component of a CAD system for mammographic interpretation.

This project aims at developing a novel interval change analysis scheme to improve the accuracy of CAD. We will investigate the problem of classifying microcalcifications as

malignant or benign based on temporal changes in mammographic features using a combination of computer vision, automated feature extraction, statistical classification, and artificial intelligence techniques. We hypothesize that the use of temporal information would improve the ability of CAD to offer an accurate and objective second opinion to radiologists which, in turn, would increase the positive predictive value of mammography, reduce the number of benign biopsies, and hence reduce both cost and patient morbidity. If integrated in a complete CAD system, the algorithms to be developed in this project may also increase the efficacy of mammography for early detection of breast cancer.

(5) Body

In the third year (7/1/04-6/30/05) of this grant, we have performed the following studies:

(A) Database collection of malignant and benign breast microcalcification cases that have multiple examinations (Task 1)

We continued collecting the data set for this study from the files of patients who had undergone biopsy at the University of Michigan. The mammograms are scanned and the images are saved in our storage device using automated graphic user interface developed in our laboratory. Additionally the film information is recorded in a Microsoft Access database. Temporal pairs of images were obtained. The current mammogram of each temporal pair exhibited a biopsy-proven mass. We scan both cranio-caudal (CC) and mediolateral-oblique (MLO) views. The mammograms were digitized with a LUMISCAN 85 laser scanner at a pixel resolution of 0.05 mm x 0.05 mm and with 12-bit resolution.

While the regional registration technique can be used for determining a corresponding structure or region for any structure (both normal tissues and masses) in the breast, in this study we are analyzing its accuracy on biopsy-proven masses alone. The location of the mass on the current mammogram is identified by an Mammography Quality Standards Act (MQSA)-approved radiologist experienced in breast imaging using an interactive image analysis tool on a UNIX workstation. To provide the ground truth for evaluation of the computerized method, the radiologist manually identifies the corresponding region on the prior mammogram. Bounding polygons enclosing the microcalcification cluster on the current mammogram and the corresponding object on the prior mammogram are provided by the radiologist for each case. Each microcalcification cluster as well as the corresponding structure on the prior mammogram are rated for its visibility on a scale of 1 to 10, where the rating of 1 corresponded to the most visible category. The size of the microcalcification cluster on the current mammogram as well as the size of the corresponding structure on the prior mammogram are also measured by the radiologist. The parenchymal density is rated based on the Breast Imaging Reporting and Data System (BI-RADS) lexicon.

(B) Development of a regional registration technique for localization of a search region for the corresponding microcalcification cluster on the prior mammogram of the same view. (Task 2)

We continued the development of a multistage regional registration technique for identifying corresponding microcalcification clusters on temporal pairs of mammograms. This detection approach mimics the method used by radiologists for searching corresponding lesions

on mammograms, i.e., the lesion is searched at approximately the same radial distance from the nipple on both views, and feature comparison will be used for further identifying the matching lesion. In the first stage, an initial search region was estimated on the prior mammogram based on the lesion location on the current mammogram. In the second stage the search region was refined. In the third stage the lesion was detected within the search region.

Initially, the breast image was segmented from the background in the current and prior mammograms. We used the methods already developed in out lab, which work reliably for segmentation of the breast image from the background for our automated detection algorithms for single images [1], [2].

For the first stage of the multistage regional registration technique we need the nipple location on the current and prior mammograms. We are in the process of developing an automated nipple detection program. Currently its accuracy is about 85% in a data set of 744 images (91% for 599 images with visible nipple and 62% for 145 images with invisible nipple) [3]. However, at this time we used manually marked nipple locations on the mammograms. We are still working to further improve the accuracy of the nipple detection algorithm aiming its use into the initial step of our automated interval change analysis scheme.

Initial global alignment of mammograms

In the first stage of registration, an initial fan-shaped search region is automatically defined on the prior mammogram based on the cluster location on the current mammogram. The cluster on the current mammogram can either be detected by an automated program or selected interactively by a radiologist. Currently we used the markings of the cluster locations given by the radiologist.

In this year of the project, for the initial estimation of the lesion centroid location on the prior mammogram we used our regional registration method (RRM) [4][5], based on the radial distance between the nipple and the lesion centroid and the angular distance between the nipple-lesion centroid axis and the breast boundary on the current mammogram. This selection was based on the results obtained during the first and second year of the project and reported in [6].

Currently we are testing a generalization of the RRM, where a number of corresponding "nipple locations" are generated both on current and prior mammograms. The RRM method is then applied for each of the locations. The final prediction of the location of the microclcification cluster on prior will be the average of all predicted points from the different "nipple locations". This method seems promising to improve the precession of the predicted location of the cluster on prior mammogram and we are going to continue its development and evaluation.

We will continue our studies to improve the technique and evaluate its accuracy on a

larger data set. We are going also to evaluate the performance of the RRM based on automatic nipple detection.

(C) Adaptation of the automated detection method for identification of candidates of microcalcification clusters within the search region. (Task 3)

We continued working on the adaptation of the automatic microcalcification detection for identification of mirocalcification clusters within a small search region. The search region (ROI) estimates the area that the cluster is most likely located but it does not provide the exact location. As the next step, automated detection of microcalcification cluster within the search region is performed. Our current automated microcalcification detection algorithm [7] provides a basis for this search. Since the detection is limited to the small search region, the algorithm parameters can be adjusted to improve the detection sensitivity of the very subtle clusters on the prior mammograms without excessive trade-off in increasing false-positives (FPs).

In the second stage of the registration technique, we investigated the possibility of detection of cluster candidates within the search region with our automated cluster search program with increased sensitivity. We performed tuning of the cluster search program by adjusting the signal to noise threshold (SNR), minimum and maximum values for the number of detected signals, the neural network output threshold. We observed that with higher values for the minimum and maximum limits for the number of detected signals (i.e. allowing larger number of detected signals), and using higher neural network output threshold we obtained better sensitivity with smaller number of FP.

Using our conventional current cluster detection program with standard thresholds and 100 um images, 76.6% (134/175) of the clusters (TP) with an average of 0.45 false positives (FP) were detected within the search region on the prior mammogram.

Using a high-sensitivity threshold and parameters and 100 um images, the cluster search program detected 89.1% (156/175) of the true clusters (TP) with an average of 0.43 false positives (FP) cluster within the search region on the prior mammograms.

During the past year we have adapted the program to use 50 um images by retraining the parameters of the detection algorithm for 50 um pixel size to optimize its accuracy. The retraining was based on hand selected individual microcalcification locations from experienced medical physicist on 57 prior mammograms.

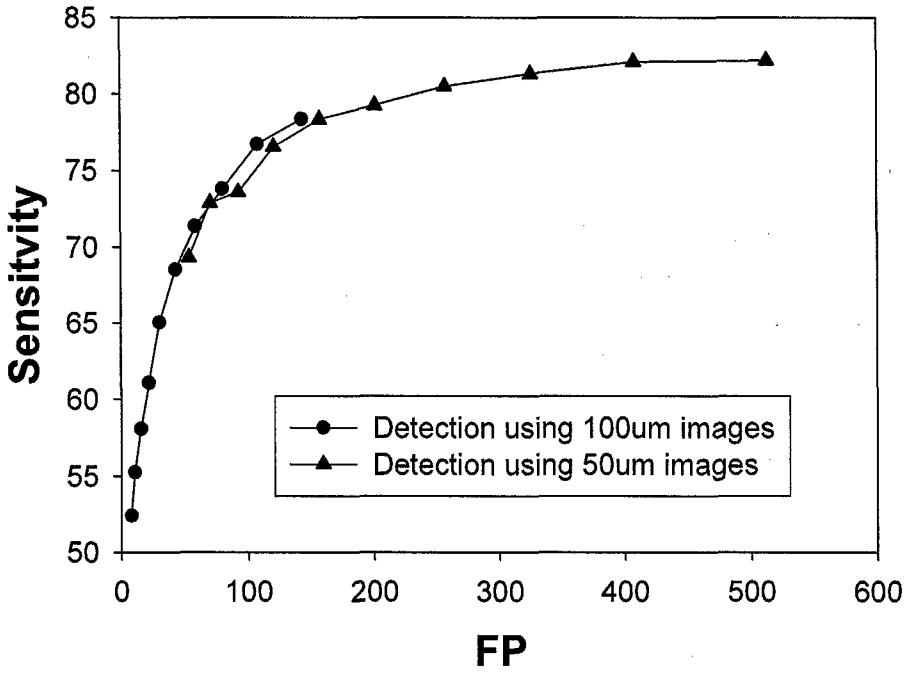

Figure 1. Detection results for the two algorithms optimized to detect microcalcifications on 100um and 50um images respectively. The FP rate is for individual calcs and it is averaged per image.

Using the subset of the 57 prior mammograms with the hand selected individual microcalcification locations we evaluated also the performance of the detection algorithm both for 50 um and 100um mammograms. We selected the set of best parameters for each system. The detection results are presented on Figure 1. We can observe that there was no improvement in the case when we used detection on 50um images in the range of reasonable FP rate (FP per individual microcalcifications).

We continued optimizing the parameters and thresholds for the detection on 100um images. Using an optimized high-sensitivity thresholds and parameters for the 100 um images, the cluster search program detected 90.3% (158/175) of the true clusters (TP) on the priors with an average of 0.43 false positives (FP) cluster within the search region on the prior mammograms. These results show slight improvement in the detection rate for the cluster search program using 100um images and the optimized set of parameters and thresholds.

The above results are summarized in Table 1.

Table 1. Detection results within the local search area.

Detection type	TP [%]	FP/image
Conventional cluster detection program, Standard thresholds, 100 um image	76.6%	0.45
Cluster search program, High-sensitivity threshold and parameters, 100 um image	89.1%	0.43
Cluster search program, Optimized high-sensitivity threshold and parameters, 100 um image	90.3%	0.43

We will present these results at RSNA 2005 [8].

We will continue to investigate the possibilities to increase the sensitivity without increasing substantially the FP within the search region in order to detect more very subtle clusters.

(D) Feature extraction techniques and definition of similarity measure for matching corresponding microcalcification clusters on current and prior mammograms (Task 4)

The cluster (TP) on the current image was paired with every detected cluster (TP or FP) in the search region to form (TP-TP) and (TP-FP) pairs. Texture and morphological features were extracted from the clusters on the current and the prior mammograms.

We continued working on the improving the feature extraction techniques. We adapted and optimized the feature extraction program to extract morphological features from microcalcification clusters in 50um images. The higher resolution images (50um) contain more precise shape information for the individual microcalcifications, which potentially can result in better quality morphological features. We extracted morphological features such as area, contrast, axis ratio and eccentricity of an effective ellipse, and moments of the individual microcalcifications and their statistics within a cluster such as the mean, standard deviation, or histogram shape (e.g., skewness and kurtosis). The extracted texture features were calculated from the spatial gray-level dependence (SGLD) matrices [9], and from the gray level difference statistics (GLDS) [10, 11]. These texture features describe characteristics such as contrast, local homogeneity, and regularity

in the image. The texture features were extracted from the cluster area on 100um images.

Difference similarity measure was derived from the extracted features of the TP or FP clusters for each temporal pair. We formed the following similarity measures between the current and prior features for each individual feature: the difference, the absolute difference, the squared difference, and the Euclidean distance.

We compared the performance of above similarity measures for the design of the correspondence classifier which is reported in the next section.

We will continue the design of new types of features and similarity measures. We studied a number of similarity measures for the task of template matching of a template containing a current lesion (current mammogram) within the search region on prior mammogram containing the prior lesion, which is closely related to correspondence classifier reduction of TP-FP pairs . We found that correlation, cosine and Gamma similarity measures outperformed similarity measures such as mutual information. The results of this study are published in Medical Physics [12].

We started investigating how useful the correlation, cosine, and Gamma similarity measures, which showed a great promise for template matching, are going to be in the case of the correspondence classifier.

(E) Design of a correspondence classifier for identification of matched cluster pairs (Task 5)

In the final stage, a correspondence classifier was designed to reduce the false pairs (TP-FP) within the search region (Figure 2). We continued the design of a correspondence classifier. We used the above obtained difference similarity measure features as the input to the classifier. A leave-one-case-out training and testing resampling scheme was used for feature selection and classification. A stepwise feature selection with floating window of 5 was used in order to obtain a subset of effective features. We used a linear discriminant classifier to merge the selected features for classification of the TP-TP and TP-FP cluster pairs.

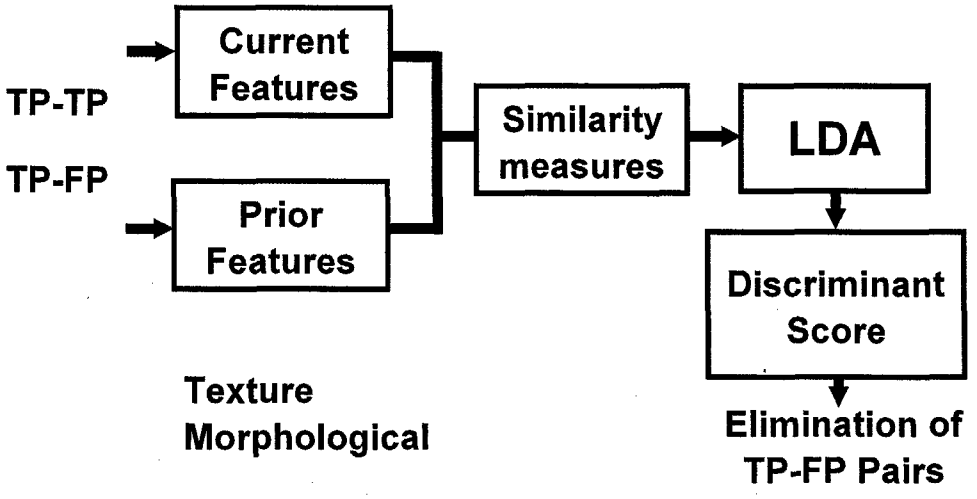

Figure 2. The correspondence classifier designed to reduce the false pairs.

The best result for the correspondence classifier was obtained for a combination of the squared difference morphological features. 6 features on average were selected. The test area under ROC curve Az, for the correspondence classifier was 0.82. The correspondence classifier reduced the FP rate to an average of 0.15 FP cluster with sensitivity of 85% (149/175) (Table 2). This improved result compared to our previous report and study [13] is due to the improved quality of the morphological features. These results will be presented at RSNA 2005 [8].

Table 2. Results for the correspondence classifier.

Number of features	A_z	TP [%]	FP/image
6	0.82	85%	0.15

In the future year we will continue studying and developing different classifiers and ways to represent the correspondence information between prior and current TP and FP clusters.

(F) Development of feature measures and temporal classifier for characterization of temporal changes in microcalcification clusters. (Task 6)

In the past year of the project we made a major progress in the direction of designing an automatic CAD system for characterization of temporal cases on malignant and benign. This is very novel and unique CAD system which includes an automatic registration of the corresponding

current and prior clusters and then classifying them by a temporal classifier on malignant and benign (Figure 3). For this purpose the feature extraction and classification were carried out with the clusters and individual microcalcifications obtained automatically from the registration stage. The design of an automatic CAD also presents challenges. The automatically detected cluster locations on the temporal pairs may deviate from the optimal locations as selected by expert radiologists. This will introduce "noise" to the extracted features and make the classification task more difficult.

Feature extraction and definition of difference features

In this study, a new classification scheme using interval change information was developed to classify mammographic microcalcification clusters as malignant and benign (Figure 3).

From each automatically detected cluster, 20 run length statistic texture features (RLSF) and 21 morphological (Mo) features were extracted [14]. Additionally, 78 SGLD [9] and 64 GLDS [10, 11] texture features were also extracted. All texture features (RLSF, SGLD, and GLDS) were extracted from automatically detected cluster locations. The morphological features were extracted from the automatically detected microcalcifications within the automatically detected cluster locations.

Twenty difference RLSF were obtained by subtracting a prior RLSF from the corresponding current RLSF. We have designed a new feature, the ratio feature, which is defined as the ratio between current and prior feature. We have obtained 21 Mo ratio features. In addition we used current GLDS features.

Table 3. The feature vector used for the temporal classifier.

Generated feature type	Ratio features	Difference features	Current features
Features	Mo	RLSF	GLDS
Number of features	21	20	64

The feature space consisted of the Mo ratio features, the difference RLSF, as well as the current GLDS features (Table 3).

Classifier design

When we are designing the classification system for classification of microcalcification clusters on malignant and benign we have to consider the fact that the microcalcification detection

algorithm may not be able to detect all clusters on prior. If the cluster is very subtle the automatic microcalcification detection for the identification of mirocalcification clusters may not be able to detect it. In this case two types of classifiers are designed. A temporal classifier (Figure 3) based on current and prior information is used if a cluster is detected in the prior, and a current classifier (Figure 4) based on current information alone is used if no prior cluster is detected. The temporal classifier is trained to classify the true (TP-TP) and false (TP-FP) pairs. The automatically detected cluster locations on the temporal pairs may deviate from the optimal locations as selected by expert radiologists. This will introduce "noise" to the extracted features and make the classification task more difficult. A linear discriminant analysis classifier (LDA) and stepwise feature selection with floating window of 3 were used to select the most useful feature subsets and to merge the features into a discriminant score (Figure 3 and Figure 4). A leave-one-case-out resampling scheme was used for feature selection and to train and to test the LDA classifiers. The current classifier was trained using the current images from the temporal pairs (the cases that has detection on prior) and tested on the cases that have not detection on prior. The classification accuracy was analyzed by receiver operating characteristic (ROC) methodology.

In this study, 175 serial pairs containing biopsy-proven calcification clusters were used. On the priors, the radiologist rated 12 of the 175 clusters as not visible and the subtlety of 18 clusters as 9 or 10 on a scale of 10.

The correspondence classifier identified 85% (149/175) of the TP-TP pairs with 15 false matches (TP-FP) within the 164 image pairs that had detected clusters. For the temporal classifier an average of 7 features were selected (Table 4). The selected features included 1 difference RLS feature, 4 morphological ratio features and 2 GLDS features from the current image. All the features were consistently selected for all the training partitions. The temporal classifier achieved a test Az of 0.83 for the 164 pairs for classifying the clusters as malignant or benign (Table 5).

For the current classifier that was classifying 11 clusters without detection on the prior, an average of 6 features from the current images were selected (Table 4). The selected features included 1 current RLS feature, 3 current morphological features and 2 GLDS current features. All the features were consistently selected for all the training partitions. The test Az by the current classifier was 0.72 for classifying the clusters as malignant or benign (Table 5).

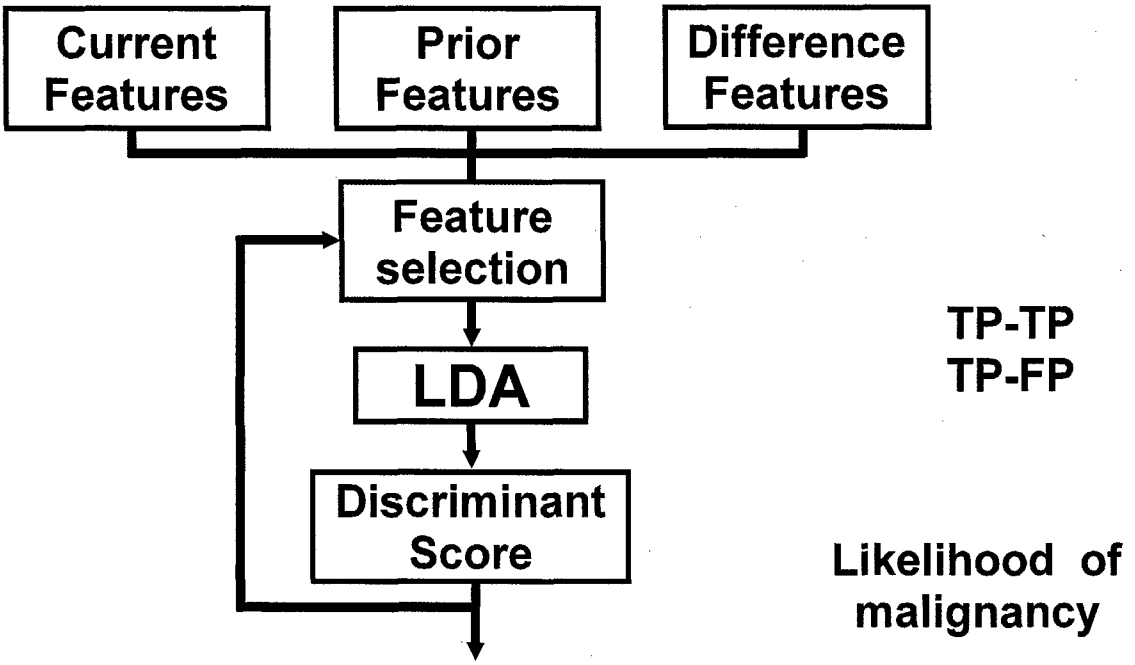

Figure 3. Temporal classifier for classification of temporal pairs of microcalcification clusters on malignant and benign.

The difference RLS texture features, morphological ratio features and GLDS current features were useful for identification of malignancy in temporal pairs of mammograms. The information on the prior image improved characterization of the microcalcification clusters: 5 out of the 7 selected features contained prior information.

Table 4. Selected features for the combined classifier for classification on malignant and benign of automatically detected clusters in current and prior mammograms.

Classifier	Feature type	Ratio features	Difference features	Current features
Temporal classifier	Mo	4		
	RLSF		1	
	GLDS			2
Current classifier	Mo			3
	RLSF			1
	GLDS			2

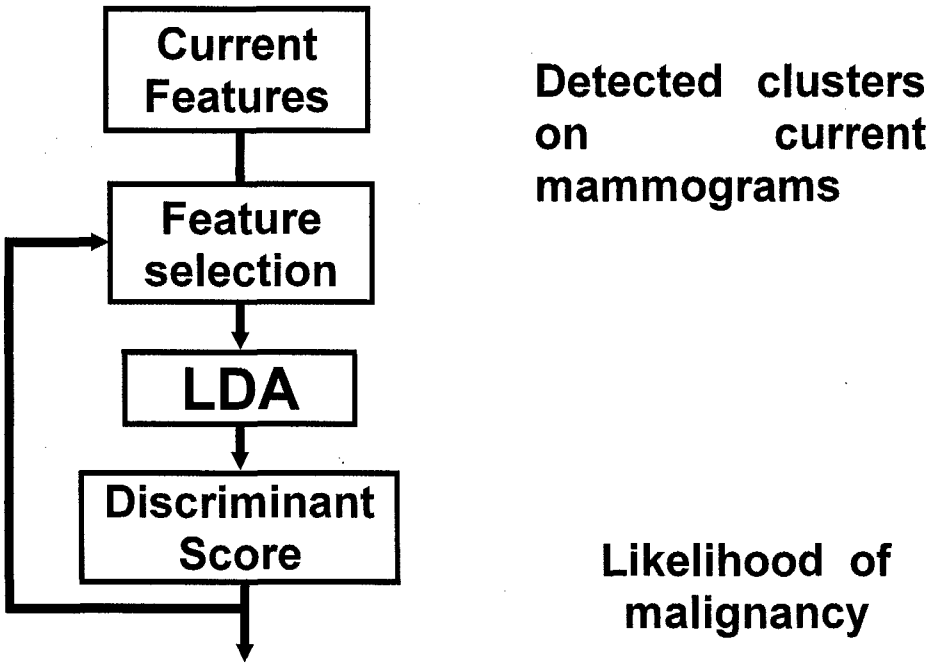

Figure 4. Current classifier based on current information alone. It is used in the case if no prior cluster is detected.

Table 5. Results for the combined classifier for classification on malignant and benign of automatically detected clusters in current and prior mammograms.

Classifier Type	Temporal classifier	Current classifier
No. of pairs (or only current images)	164	11
Number of selected features	7	6
Az	0.83	0.72

In the future year we will continue to develop, improve and compare classification approaches in order to classify the clusters on malignant and benign based on automatically detected clusters and individual microcalcifications.

(G) Compare the classification accuracy of the classification scheme using temporal change information with that of a classifier using single-exam information alone. (Task 7).

We started performing a comparison between the temporal classifier and classifier based on current images. The test A_z for the classifier based on 164 current images was 0.75. We see an improvement for the temporal classifier (A_z=0.83) when compared to the current classifier. We will continue to perform comparisons for the different design of both the temporal pair classifiers and the current classifiers.

(H) Conduct observer performance study to compare radiologists' classification of malignant and benign microcalcifications with and without the aid of the temporal change classifier. (Task 8).

We started performed a pilot study as a first step to design an observer performance experiment with ROC methodology to evaluate the effects of computer classification on radiologists' estimates of the likelihood of malignancy of temporal pairs of microcalcification clusters. A graphical user interface was developed on a PC to display side-by-side the temporal pairs of masses in a predesigned random order for each observer. The likelihood of malignancy and the BI-RADS assessment of the radiologist on each pair is automatically recorded when they select it on a slider.

175 temporal image pairs (51 malignant and 124 benign) containing microcalcification clusters on serial mammograms were chosen from patient files and digitized. The true microcalcification cluster locations were identified by an experienced radiologist on all mammograms. All cases eventually underwent biopsy so that interval change was observed for most of the microcalcification clusters even if they were found to be benign after biopsy. This was therefore a difficult data set for interval change analysis. We have selected additional 32 biobsied cases with multiple exams which are digitized and the radiologist is in a process of identifying the microclacification cluster locations.

One MQSA radiologists assessed the temporal pairs that were displayed on the display PC workstation. They provided estimates of the likelihood of malignancy and BI-RADS assessment without CAD. The reading order of the temporal pairs was randomized. The classification accuracy was quantified by using the area under ROC curve, A_z.

The MQSA radiologist achieved an Az of 0.72 for both all 175 temporal pairs and also for the subset of 164 temporal pairs with automatic cluster detection on prior.

This pilot study indicates that CAD using interval change analysis were able to classify the automatically detected temporal pairs of microcalcification clusters with accuracy comparable to

that of an experienced radiologist and may be useful for assisting radiologists in classification of masses and thereby reducing unnecessary biopsies.

This pilot study will be the basis for our design of a full-scale ROC study, were the radiologists will provide estimates of the likelihood of malignancy and BI-RADS assessment also with CAD. We are in process of recruiting breast radiologists at our department to participate as observers. The sample size is acceptable but we are continuing to enlarge the data set until the ROC study design is finalized. We expect that this ROC study can be completed within the no cost time extension year approved for this grant. This type of observer study is new and unique and the outcome will be important, providing a new understanding of the potentials of computer aid to the radiologists in characterization of the temporal changes of mammographic masses.

(6) Key research accomplishments in current year as a result of this grant

- Increase of the temporal microcalcification database (collection of new temporal cases and extraction of regions of interest) (Task 1).
- Selection of RRM method for establishing corresponding locations in current and prior mammograms as most accurate compared to the linear and nonlinear warping methods (Task 2).
- Successful adaptation of the automated detection method for identification of candidates of microcalcification clusters within the search region to high sensitive mode (Task 3).
- Improvement of the morphological feature extraction (using 50um images) for matching corresponding microcalcification clusters on current and prior mammograms (Task 4).
- Extraction of RLS, GLDS and morphological features from automatically detected clusters and individual microcalcifications.
- Improvement of the design of the correspondence classifier for identification of matched cluster TP-TP pairs, that improved sensitivity and specificity of the cluster detection based on squared difference similarity measures and morphological features (Task 5).
- Definition of new difference similarity measure (ratio features) for morphological feature measures for characterization of temporal changes in microcalcification clusters (Task 6).
- Development of the classifier for classification on malignant and benign clusters based on automatically detected clusters and individual microcalcifications (Task 6).
- Initial comparison of temporal classifier and classifier based on current microcalcification clusters (Task 7).
- Performing a pilot observer study with the radiologist evaluating temporal pairs of microclacification clusters without CAD (Task 8).

(7) Reportable Outcomes

Publications in current year as a result of this grant

[1] Hadjiiski LM, HP Chan, B Sahiner, MA Helvie, MA Roubidoux, C Zhou, "Interval change analysis based on computerized regional registration of corresponding microcalcification clusters on temporal pairs of mammograms," *90th Scientific Assembly and Annual Meeting of the Radiological Society of North America*, Chicago, IL, Nov. 28-Dec 3, 2004, pp. 491.

[2] Hadjiiski LM, HP Chan, B Sahiner, MA Helvie, MA Roubidoux, C Zhou, "Automated regional registration and classification of corresponding microcalcification clusters on serial mammograms," To be presented at the *91th Scientific Assembly and Annual Meeting of the Radiological Society of North America*, Chicago, IL, Nov. 27-Dec 2, 2005.

Copies of publications are enclosed with this report.

(8) Conclusion

As a result of the support by the USAMRMC grant, in the third year of this project, we have (1) collected additional cases with temporal microcalcification clusters; (2) Applied the RRM for the localization of the search region for the corresponding microcalcification cluster on the prior mammogram; (3) Adapted the automated detection method for identification of candidates of microcalcification clusters within the search region; (4) Extracted texture and morphological features and defined difference similarity measures for matching corresponding microcalcification clusters on current and prior mammograms from automatically detected microcalcification clusters; (5) Design a correspondence classifier for identification of matched cluster based on extracted features and the difference similarity measures; (6) Develop feature measures and temporal classifier for characterization of temporal changes in automatically detected microcalcification clusters; (7) Compare the temporal classifier with classifier based on current images only; (8) Perform a pilot observer study.

The results obtained so far are encouraging. The RRM allowed to have all the clusters within the search region on the prior mammogram. We were successful to adapt and improve the automated microcalcification detection system to be more sensitive for identification of candidates of microcalcification clusters within the local search region. It was able to detect substantially more true clusters without increasing the FP rate compared to the conventional detection system and the system from previous year. The squared difference similarity measure applied to the enhanced morphological features was the successful combination for the input to the correspondence classifier. The correspondence classifier was able to reduce the TP-FP pairs resulting in less FP clusters within the search region on prior. The new classification scheme, using interval change information, to classify mammographic microcalcification clusters as malignant and benign showed promising results. Morphological ratio features, difference RLS features and current GLDS features were useful for the classification.

We have made a major progress in the direction of the ultimate goal of the project - to have an automatic CAD system for characterization of temporal cases on malignant and benign. For that purpose a feature extraction and classification was carried out with the clusters and individual microcalcifications obtained automatically from the registration stage. Based on these features we have designed a classification scheme to classify the automatically registered and detected microcalcification clusters. This temporal classifier performed better than the classifier based on current images only. We performed a pilot observer study for evaluation of the radiologist performance without CAD. The classification scheme was able to classify the automatically detected temporal pairs of microcalcification clusters with accuracy comparable to that of an experienced radiologist.

The design of an automatic CAD can also presents challenges. The automatically detected cluster locations on the temporal pairs may deviate from the optimal locations as selected by expert radiologists. This will introduce "noise" to the extracted features and make the classification task more difficult. In the feature year we will continue to improve all the stages of the automatic detection and classification system with the aim to improve the classification results for microcalcification clusters obtained automatically from the registration stage.

(9) References

1. Petrick N, Chan HP, Wei D, Sahiner B, Helvie MA and Adler DD, "Automated detection of breast masses on mammograms using adaptive contrast enhancement and texture classification," Med Phys 23, 1685-1696 (1996).
2. Zhou C, Chan H, Petrick N, Helvie M, Goodsitt M, Sahiner B and Hadjiiski L, "Computerized image analysis: Estimation of breast density on mammograms.," Med Phys.,28 (6), June (2001) pp. 1056-1069.
3. Zhou C, HP Chan, C Paramagul, MA Roubidoux, B Sahiner, LM Hadjiiski, N Petrick, "Computer-aided diagnosis on mammograms using multiple image analysis: computerized nipple identification," *Med Phys,* 2004, 31 (10), 2871-2882.
4. S.S. Gopal, H.P. Chan, T.E. Wilson, M.A. Helvie, N. Petrick, B. Sahiner, "A regional registration technique for automated interval change analysis of breast lesions on mammograms", *Medical Physics,* 1999, 26:2669-2679.
5. L. Hadjiiski, H.P. Chan, B. Sahiner, N. Petrick, M. Helvie, "Automated Registration of Breast Lesions in Temporal Pairs of Mammograms for Interval Change Analysis – Local Affine Transformation for Improved Localization", *Medical Physics*, 28 (6), June 2001, pp. 1070-1079.
6. L. Hadjiiski, H.P. Chan, B. Sahiner, C Zhou, M.A. Helvie, M.A. Roubidoux, "Computerized Regional Registration of Corresponding Masses and Microcalcification Clusters on Temporal Pairs of Mammograms for Interval Change Analysis", *89th Scientific Assembly and Annual Meeting of the Radiological Society of North America (RSNA)*, Chicago, Illinois, 2003.
7. Chan HP, Lo SCB, Sahiner B, Lam KL and Helvie MA, "Computer-aided detection of mammographic microcalcifications: Pattern recognition with an artificial neural network," Med Phys 22, 1555-1567 (1995).

(8). Hadjiiski LM, HP Chan, B Sahiner, MA Helvie, MA Roubidoux, C Zhou, "Automated regional registration and classification of corresponding microcalcification clusters on serial mammograms," To be presented at the *91th Scientific Assembly and Annual Meeting of the Radiological Society of North America*, Chicago, IL, Nov. 27-Dec 2, 2005.

(9). Haralick RM, Shanmugam K and Dinstein I, "Texture features for image classification," IEEE Trans Sys Man and Cybern SMC-3, 610-621 (1973).

(10). Sahiner B, Chan HP, Petrick N, Wei D, Helvie MA, Adler DD and Goodsitt MM, "Classification of mass and normal breast tissue: A convolution neural network classifier with spatial domain and texture images," IEEE Trans Med Img 15, 598-610 (1996).

(11). Weszka JS, Dyer CR and Rosenfeld A, "A comparative study of texture measures for terrain classification," IEEE Trans Sys Man and Cybern 6, 269-285 (1976).

(12). Filev P, LM Hadjiiski, B Sahiner, H-P Chan, MA Helvie, "Comparison of similarity measures for the task of template matching of masses on serial mammograms," *Med Phys* 2005, 32 (2), 515-529.

13. Hadjiiski LM, HP Chan, B Sahiner, MA Helvie, MA Roubidoux, C Zhou, "Interval change analysis based on computerized regional registration of corresponding microcalcification clusters on temporal pairs of mammograms," *90th Scientific Assembly and Annual Meeting of the Radiological Society of North America*, Chicago, IL, Nov. 28-Dec 3, 2004, pp. 491.

14. L. Hadjiiski, H.P. Chan, M. Gurcan, B. Sahiner, N. Petrick, M.A. Helvie, M. Roubidoux "Computer-Aided Characterization of Malignant and Benign Microcalcification Clusters Based on the Analysis of Temporal Change of Mammographic Features", Presented at the *SPIE International Symposium on Medical Imaging*, San Diego, California, February 23-28, 2002. *Proc. SPIE Medical Imaging, 2002, 4684, pp.749-753.*

(10) Appendix

Copies of publications are enclosed with this report.

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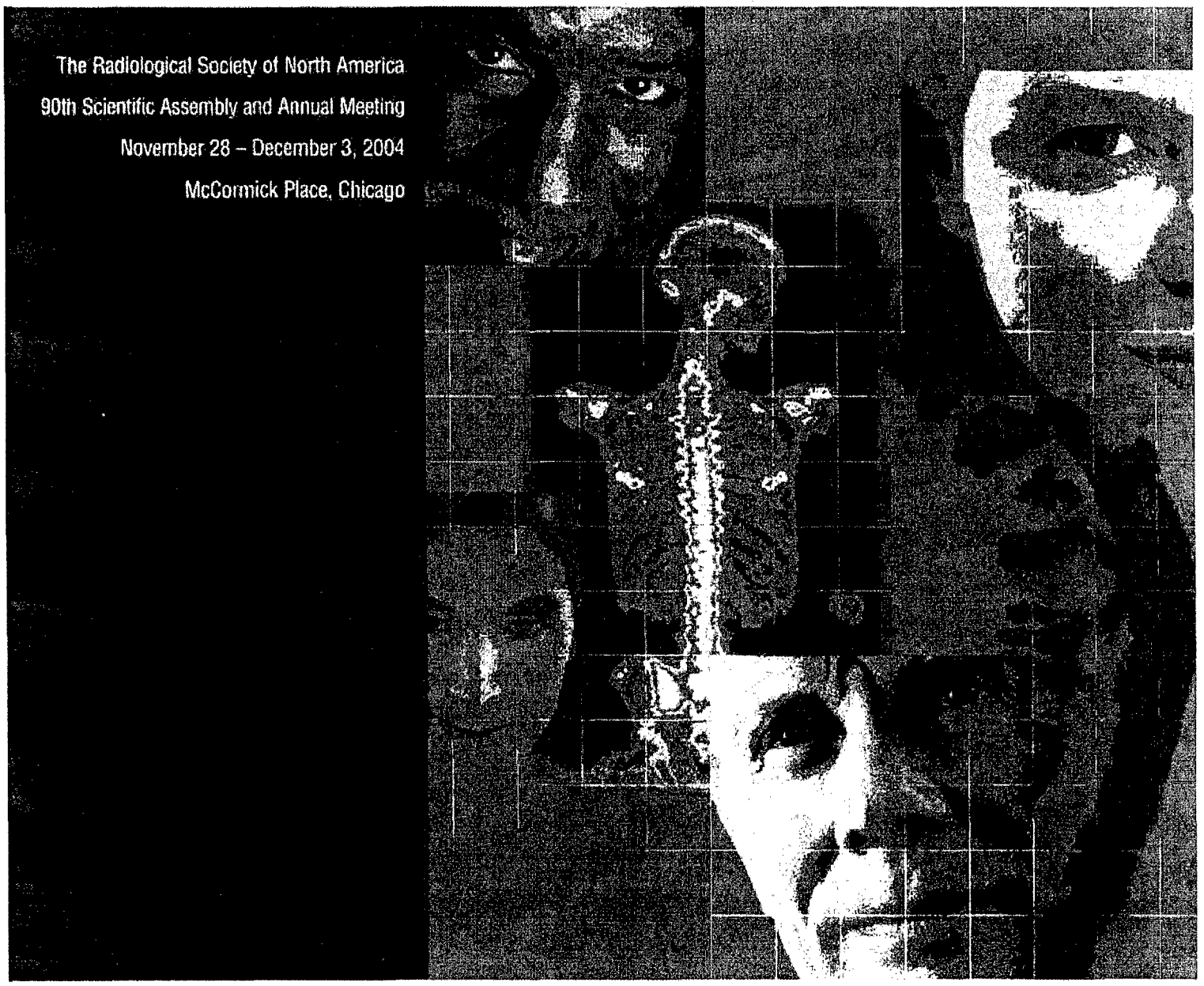

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SSJ17-01 • 3:00 PM

ual Computer-aided Detection (CAD) System for Improvement of Mass ction on Mammograms

s, PhD, Ann Arbor, MI • B. Sahiner, PhD* • L.M. Hadjiiski, PhD* • H. , PhD* • M.A. Helvie, MD* • M.A. Roubidoux, MD**

POSE: To develop a dual CAD system which combines a regular CAD em with a new system trained with masses seen on retrospective ew of prior mammograms to improve its performance for detecting e masses.

HOD AND MATERIALS: A data set of 109 patients containing 211 nt mammograms with biopsy-proven masses and 261 prior mammo- s was used. We randomly divided the data set into two independent for both the current and prior mammograms: the training set ned 54 cases and the test set contained 55 cases. Two single CAD ms were trained, one with current mammograms and the other with r mammograms. A two-stage gradient field analysis was used to reen for mass candidates in both CAD systems. The suspicious ture in each identified region was extracted by clustering-based n growing. Morphological and spatial gray-level dependence texture ures were extracted from the current mammograms. For detection of subtle masses on the prior mammograms, histogram and run-length stics features were extracted. Stepwise linear discriminant analysis A) with simplex optimization was used to select the most useful es. Finally, rule-based and LDA classifiers were used to differentiate es from normal tissues. When the dual CAD system was applied to a e mammogram, the detection information by the two CAD systems on me mammogram were merged with a fusion scheme.

ULTS: When the single CAD system trained on current mammograms pplied to the test sets, the case-based sensitivities were 87% and 65% urrent mammograms and 50% and 30% on prior mammograms at 2 l FPs/image, respectively. When the single CAD system trained with r mammograms was used, the case-based sensitivities were 81% and on current mammograms and 56% and 46% on prior mammograms at d 1 FPs/image, respectively. With the dual CAD system, the case- d sensitivities were improved to 89% and 75% on current mammo- ms and 60% and 48% on prior mammograms at the same FP rates.

CLUSIONS: The dual CAD system improved the overall detection rmance for all masses. Further work is underway to optimize the n scheme in the dual CAD system.

SSJ17-02 • 3:10 PM

rmination of the Degree of Subjective Similarity for Pairs of Clustered rocalcifications on Mammograms: Preliminary Observer Study

ramatsu, Chicago, IL • Q. Li, PhD* • R.A. Schmidt, MD • K. Suzuki, * • G.M. Newstead, MD* • K. Doi, PhD (chisa@uchicago.edu)*

POSE: Presentation of similar images should be useful for radiologists e distinction between benign and malignant clustered microcalcifica- s on mammograms. The purpose of this study was to determine ologists' subjective similarity which could then be used as a gold dard for evaluation of objective similarity measures for automated ion of similar images.

THOD AND MATERIALS: A total of 884 (504 benign and 380 malig- regions of interest (5 cm x 5 cm) for biopsy-proven clustered rocalcifications was obtained from the Digital Database for Screening mography organized by the University of South Florida. An observer y was conducted to obtain subjective similarity ratings for 114 pairs of ered microcalcifications on mammograms. Six image pairs were d on a high resolution LCD monitor such that one image in the center compared to three images each on the right and left side. Pathologies sions were not revealed to observers. Ratings were marked on a continuous rating scale between 0 and 1, where 0 and 1 correspond to images not similar at all and almost identical, respectively. Nine breast radiologists, ten general radiologists, and nine non-radiologists participated in the study; some of them completed multiple times. Correlation values between two observers, groups of observers, and individual observers were determined.

RESULTS: Inter- and intra-observer correlation values varied from 0.021 to 0.602 and 0.408 to 0.721, respectively. Correlation values between two breast radiologists were generally higher than those between two general radiologists. When similarity ratings were averaged for breast radiologists and general radiologists, the correlation value between the two groups became 0.857, which is considered reasonably high.

CONCLUSIONS: The variation in similarity ratings between two individuals was not small. However, when a number of reliable observers provide similarity ratings, average ratings may be used as a gold standard for development of objective similarity measures to select similar images that we expect will be useful for radiologists in the diagnosis of clustered microcalcifications on mammograms, a task difficult for most radiologists. (K.D.: Author is shareholder of Deus Technology Inc., Rockville, MD K.D.,R.A.S.: Authors are shareholders of R2 Technology Inc., Los Altos, CA)

SSJ17-03 • 3:20 PM

Interval Change Analysis Based on Computerized Regional Registration of Corresponding Microcalcification Clusters on Temporal Pairs of Mammograms

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PURPOSE: To develop an automated method for characterization of microcalcification clusters using interval change information on serial mammograms. This analysis will be useful for identification of new or growing clusters in a detection system or for classification of malignant and benign clusters in a diagnostic system.

METHOD AND MATERIALS: The automated interval change analysis method consisted of two stages: (1) detection of corresponding cluster on the prior, and (2) classification of cluster as new, growing, or stable. In the first stage, based on the position of a detected cluster on the current mammogram a regional registration procedure identified the local area that might contain the corresponding cluster on the prior. A search program was used to detect cluster candidates within the local area. The cluster on the current mammogram was then paired with the detected candidates to form (TP-TP) and (TP-FP) pairs. Features were automatically extracted and a correspondence classifier was designed to reduce the false pairs (TP-FP). In the second stage, the current cluster is classified as new if no cluster is detected in prior, or the detected clusters will be classified as growing or stable based on analysis of the current and prior pairs. In this study, we focussed on the first stage. 175 serial mammogram pairs containing biopsy-proven clusters on current mammograms were used. An MQSA radiologist identified the corresponding clusters on the mammograms. On priors, the radiologist rated 12 of the 175 clusters as not visible and the subtlety of 18 clusters as 9 and 10 on a scale of 10. A leave-one-case-out resampling scheme was used for feature selection and classification.

RESULTS: The search program detected 89% (156/175) of the clusters with an average of 0.43 FP cluster on priors. The correspondence classifier identified 81% (141/175) of the TP-TP pairs with 21 false matches within the 162 image pairs that had detected clusters.

CONCLUSIONS: Our study demonstrated that our registration and matching technique can find the corresponding cluster on the prior with high sensitivity, considering many of the clusters were very subtle. This is a promising step for automated analysis of clusters on serial mammograms.

SSJ17-04 • 3:30 PM

Computer-aided Diagnosis Scheme for Identifying Histological Classification of Clustered Microcalcifications Using MLO and CC Magnification Mammograms

FDA

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PURPOSE: It is difficult to make correct clinical decisions for biopsy or follow-up on clustered microcalcifications on mammograms. The purpose of this study was to develop a computer-aided diagnosis scheme for identifying histological classification of clustered microcalcifications on magnification mammograms in order to assist radiologists' interpretation as a "second opinion."

METHOD AND MATERIALS: Our database consisted of mediolateral oblique (MLO) and craniocaudal (CC) magnification mammograms (512x512 pixels, 12bit/pixels, 0.0275mm/pixel) obtained from 56 patients, which included 38 malignant clustered microcalcifications (invasive carcinoma, noninvasive carcinoma of comedo type, and noninvasive carcinoma

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Primary Category: Physics
Secondary Category: Image Processing, CAD, etc

06) Automated Regional Registration and Classification of Corresponding Microcalcification Clusters on Serial Mammograms

L M Hadjiiski, PhD, Ann Arbor, MI; H Chan, PhD; B Sahiner, PhD; M A Helvie, MD; M A Roubidoux, MD; C Zhou, PhD (lhadjisk@umich.edu)

PURPOSE

To develop an automated system for detecting corresponding microcalcification clusters on serial mammograms, and classifying the cluster as malignant and benign using interval change information.

METHOD AND MATERIALS

Our system consists of two stages. In the first stage, based on the location of a detected cluster on the current mammogram, a regional registration procedure identifies the local area on the prior that may contain the corresponding cluster. A search program is used to detect cluster candidates within the local area. The cluster on the current image is then paired with the candidates to form true (TP-TP) or false (TP-FP) pairs. A correspondence classifier using automatically extracted features is designed to reduce the false pairs. In the second stage, a temporal classifier based on current and prior information is used if a cluster is detected in the prior, and a current classifier based on current information alone is used if no prior cluster is detected. In this study, 175 serial pairs containing biopsy-proven calcification clusters were used. An MQSA radiologist identified the corresponding clusters on the mammograms. On the priors, the radiologist rated 12 of the 175 clusters as not visible and the subtlety of 18 clusters as 9 or 10 on a scale of 10. Leave-one-case-out resampling was used for feature selection and classification.

RESULTS

The search program detected 90.2% (158/175) of the clusters on the priors with an average of 0.43 FPs/image. The correspondence classifier identified 85% (149/175) of the TP-TP pairs with 15 false matches within the 164 image pairs that had detected clusters. In the classification stage the temporal classifier achieved a test Az of 0.83 for the 164 pairs for classifying the clusters as malignant or benign. For the 11 clusters without detection on the prior, the test Az by the current classifier was 0.72. In comparison, the MQSA radiologist achieved an Az of 0.72 for both the 175 and the 164 temporal pairs.

CONCLUSION

Our interval change analysis system can detect the corresponding cluster on the prior mammogram with high sensitivity, and classify them with an accuracy comparable to that an experienced radiologist.

Disclosures:

No Disclosure: Heang-Ping Chan, Berkman Sahiner, Lubomir Hadjiiski, Mark Helvie, Marilyn Roubidoux, Chuan Zhou

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